REMARKS

Applicants respectfully request reconsideration of this application in view of the foregoing amendments and the following remarks.

I. Introductory Remarks

Upon entry of the foregoing amendments, claims 32-35 and 40-43 will be pending. Claims 36-39 have been canceled without prejudice or disclaimer. Claims 40-43 are new. Support for the new claims exists throughout the Specification. See, for example, page 6, lines 22-35, page 7, lines 4-12, and page 9, lines 9-12 and 19-22.

None of the new claims or claim amendments introduces new subject matter into the application.

II. Restriction Requirement

Applicants acknowledge that the Examiner has withdrawn the Restriction Requirement and has re-joined claims 32-29 for examination.

III. Specification and Claim Objections

As requested by the Examiner, the title of the specification has been amended. Claims 36-39 have been canceled without prejudice or disclaimer, mooting the Examiner's objections on pages 2-3 of the Office Action.

IV. Claims 32-39 are enabled

Claims 32-39 were rejected under § 112 because the specification while being enabling for *in vitro* methods of claims 32-39, "does not reasonably provide enablement for these methods *in vivo*." Page 3. The Examiner takes the view that: (A) the Specification does not provide guidance for "successful inhibition" of any specific condition; (B) the Specification does not provide information on the "route, duration and quantity of administration of [the claimed] antibody"; (C) "predicting the efficacy of using a given antibody that is immunoreactive for a protein as a therapeutic agent *in vivo* based solely on *prophetic suggestion* [is] highly problematic."

Applicants traverse this rejection. The Examiner is not applying the correct legal standard, based upon the state of the art. As the court held in *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), human clinical data are not required for compliance with § 112. Indeed, *in vivo* data are not required. As long as someone of skill in the art would reasonably expect that Applicant's data are predictive of the claimed use, the enablement requirement is met.

The Examiner agrees that the Specification enables *in vitro* (a) methods for inhibiting IL-5, IL-3 or GM-CSF mediated leukemic cell proliferation, using an antibody or fragment thereof of the invention and (b) methods for inhibiting IL-5, IL-3 or GM-CSF mediated

eosipophil activation, production or survival, using an antibody or fragment thereof of the invention. As explained below, based on the state of the art at the time the application was filed, the skilled artisan would reasonably expect that the antibodies and antibody fragments of the invention would also have these same activities *in vivo*. Accordingly, the skilled artisan would expect that the because of the *in vitro* results achieved by Applicants, the antibodies and antibody fragments of the invention would be useful in the treatment of diseases such as leukemia and asthma.

As explained more fully below, at the time of filing, suitable animal models for testing anti-βc antibodies against leukemia and asthma did not exist. Additionally, traditional tumor-bearing "cancer" animal models are not suitable for evaluating the inventive anti-βc antibodies for treatment of leukemia because leukemia is a disease of discrete cancerous cells which do not exist as tumors.

As explained in the Specification, at the time of filing, it was known that leukemia involves activation of at least IL-3. See Specification, page 6, lines 30-34 and U.S. Patent No. 6,177,079. It was also known that IL-5, GM-CSF, and IL-3 all play a role in eosinophil production and activation in asthma. See page 1, lines 11-31. It was further known that the receptors for all three molecules share a common β chain (βc). Therefore, as explained in the Specification, one of skill in the art would expect, based on Applicant's *vitro* data, that the inventive antibodies and antibody fragments – which target the βc - would be useful eosinophil antagonists and asthma therapeutics *in vivo*. See Specification at page 6, lines 26-30, page 7, lines 9-12. In the same vein, the skilled artisan would also expect that the inventive antibodies and antibody fragments would be useful leukemic cell antagonists and leukemia therapeutics *in vivo*. See Specification at page 6, lines 30-34; page 7, lines 4-7.

With respect to animal models, Applicant's research has shown that the human common βc is unique to humans. As described in the Specification, antibodies against human βc were generated in mice; however, the anti-βc antibodies had no adverse effects on mice and indeed, none would be expected because human βc is antigenically distinct from mouse βc. Therefore, tests of the inventive anti (human)-βc antibodies would not be expected generate clinically useful data in animal models known at the time of filing. Those

of skill in the art would therefore rely on *in vitro* data for predicting success in humans. Given what was known about the eitiology of leukemia and asthma at the time the application was filed, this was an entirely reasonable prediction.

While the Examiner also argues that antibody therapy is unpredictable, therapeutic monoclonal antibodies have been developed and sold. For example, Avastin (bevacizumab) is a marketed anti-VEGF monoclonal antibody for treating metastatic tumor-forming cancers of the colon.[1] These antibodies block VEGF-mediated angiogenesis that tumors need for their growth and proliferation.

The Examiner's focus on the alleged lack of guidance in the Specification for dosage and administration instructions is legally incorrect. The U.S. biotechnology and pharmaceutical patent literature is replete with patents claiming novel compounds and therapeutic methods, but not describing the specific dosage and administration conditions to be used. It is well known and expected in the art that such parameters must be developed at the clinical testing and commercialization stages. Indeed, it would be the rare patent that describes the dosage and administration conditions that are approved by the FDA. *Cf. CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1339 (Fed. Cir. 2003) "(Patents are not production documents, and nothing in the patent law requires that a patentee must disclose data on how to mass-produce the invented product....)" (*citing Christianson v. Colt Indus. Operating Corp.*, 822 F.2d 1544, 1562 (Fed. Cir. 1987). As discussed above, human clinical testing is not required for enablement, *Brana*, and hence description of dosing and administration regimens cannot be a requirement to satisfy § 112.

The Examiner's citation to *In Re Colianni*, 561 F.2d 220, 195 USPQ 150 (CCPA 1977) is misplaced. That case concerned a patent application filed in 1971, claiming a method for fusing bones – by administration of "sufficient" ultrasonic energy, and the application contained no working examples. The court's decision indicates that this was a novel methodology in 1971 and the court relied on the absence of working examples for its decision that the application did not meet the requirements of § 112. In contrast, the present

[1] VEGF = Vascular Endothelial Growth Factor

patent application has a 1998 priority date, and concerns therapeutic administration of a polypeptide-based therapeutic agent. As of 1998, the patent and scientific literature was replete with examples of therapeutic administration of protein-based therapeutics. Also in contrast to *Colianni*, the present application is replete with multiple working examples showing the efficacy of the claimed antibodies and antibody fragments.

Finally, Applicants disagree with the Examiner's characterization of the Specification as containing a "prophetic" suggestion to use the anti-βc antibodies *in vivo*. While U.S. law does not *per se* require any data for fulfillment of the requirements of § 112, the present Specification is replete with data on the activity of the inventive antibodies. For all the reasons discussed above, the present Specification meets the requirements of § 112 because it would not require undue experimentation to use the inventive antibodies in the claimed methods *in vivo*. Indeed, the skilled artisan would fully expect that such methods would be successful *in vivo*.

For all of the foregoing reasons, Applicants respectfully request withdrawal of the enablement rejection.

IV. Claims 32-39 are definite

The Examiner rejected the pending claims for allegedly failing to recite method steps and failing to recite a specific condition. Applicants respectfully disagree. The cancellation of claims 36-39 renders that rejection moot.

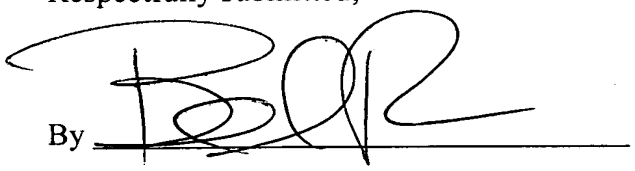
Claims 35-39 are not incomplete and do recite method steps. All claims recite the active step of "contacting" the cells (or eosinophils) with the antibody or antibody fragments. With respect to the Examiner's request that the claims recite a condition to be treated, Applicants disagree that such a recital is required for definiteness. One of skill in the art would easily understand that the inventive antibodies and antibody fragments are contacted with the cells/eosinphils to inhibit such cells – nothing more is required.

V. Concluding Remarks

Applicants believe that the present application is now in condition for allowance, and respectfully request favorable reconsideration of it. Should the Examiner believe that a telephone interview would advance prosecution, she is cordially invited to contact the undersigned attorney.

The Commissioner is hereby authorized to charge any additional fees that may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any extension fees to Deposit Account No. 19-0741.

Respectfully submitted,



Date March 27, 2007

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